REMARKS

Claims 38-43 are pending in this application. By this Amendment, claims 1-37 are canceled and claims 38-43 are added. No new matter is added. Support for new claims 38-43 can be found in the specification, for example, in the original claims.

I. NOTICE TO COMPLY

The Office Action states that the Sequence Listing fails to comply with the Patent Office's Sequence Listing Rules. Specifically, at paragraph 6, the Office Action alleges that the sequences in Table III of the instant specification are not present in the Sequence Listing. As agreed to with Examiner Li in her May 24 telephone conference with Applicants' undersigned representative, the Sequence Listing filed with the March 2, 2002, Supplemental Preliminary Amendment contains the sequences in Table III. Specifically, agreed to by Examiner Lee, SEQ ID NOs: 29-53 corresponds to the sequences in Table III. Accordingly, as agreed to by Examiner Li, submission of a new Sequence Listing (paper and computer-readable copies) is not required.

Reconsideration and withdrawal of the Notice to Comply, and acknowledgement that the sequences in Table III are present in the Sequence Listing, are respectfully requested.

II. SPECIFICATION OBJECTION

The specification is objected to for not providing sequence identifiers in Table III. By this Amendment, Table III is amended to include sequence identifiers that respectively correspond with the sequence identifiers used in the Sequence Listing. Reconsideration and withdrawal of the objection are respectfully requested.

III. RESTRICTION/ELECTION REQUIREMENT

By this Amendment, claims 1-37 are canceled in favor of new claims 38-43, which are directed to the invention of elected Group I. All of claims 38-43 are generic to the elected

species. Therefore, once the elected species is determined to be allowable, the full scope of claims 38-43 should be examined.

IV. §112, SECOND PARAGRAPH, REJECTIONS

The Office Action rejects claims 1-11 under 35 U.S.C. §112, second paragraph, as being indefinite. By this Amendment, claims 1-11 are canceled. In addition, new claims 38-43 satisfy the requirements of §112, second paragraph, for at least the reasons discussed below.

A. Claims 38-43 recite an essential method step.

The Office Action requires the recitation of an essential method step in the method claims. Claim 38 recites: "detecting a fusogenic power of said protein in cells of a cellular tissue or of a cell culture by observing formation of syncytia or an absence of formation of syncytia, wherein said detection is made in the presence of at least one cell-surface receptor." Claims 39-43 depend from claim 38 and include all of its features. Thus, all of claims 38-43 recite an essential method step, and thus satisfy the requirements of §112, second paragraph.

B. Claims 38-43 do not recite the term "preferably."

The Office Action asserts that the term "preferably" is unclear. Claims 38-43 do not recite this term. Accordingly, claims 38-43 satisfy the requirements of §112, second paragraph.

C. Claims 38-43 do not recite the phrases "at least more than 5 to 20 amino acids" and "a fragment of SEQ ID NO: 1."

The Office Action asserts that the phrases "at least more than 5 to 20 amino acids" and "a fragment of SEQ ID NO: 1" are confusing and unclear. Claims 38-43 do not recite these phrases. Accordingly, claims 38-43 satisfy the requirements of §112, second paragraph.

D. <u>The phrase "at least 95% identity with the sequence SEQ ID NO: 1" is not indefinite.</u>

The Office Action asserts that the phrase "at least 95% identity with the sequence SEQ ID NO: 1" renders claims that recite this phrase indefinite because percent homology can be calculated in a variety of ways. Claims 38 and 40-43 do not recite this phrase.

Claim 39 is directed to a method of detecting a fusogenic power of a protein in cells of a cellular tissue or of a cell culture by observing formation of syncytia or an absence of formation of syncytia, in the presence of at least one surface cell receptor. Claim 39 requires that the protein has a polypeptide sequence which exhibits at least 95% identity with the sequence SEQ ID No. 1.

MPEP §2173.02 requires that definiteness of claim language must be analyzed, not in a vacuum, but in light of the contents of the particular application disclosure, the teachings of the prior art, and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. Furthermore, MPEP §2164.01(c) states that if the specification contains within it a connotation of how to use, and/or the art recognizes that standard modes of administration are known and contemplated, 35 U.S.C. §112 is satisfied.

As acknowledged in the Office Action, various methods are known in the art for calculating percent homology. As instructed by MPEP §2173.02, the definiteness of claim 39 must be analyzed, not in a vacuum, but in light of these teachings. Because methods for calculating percent homology are known in the art, the phrase "at least 95% identity with the sequence SEQ ID NO: 1" does not render claims 39 indefinite.

Furthermore, the specification describes how to practice the method of claim 39. Specifically, the specification discloses that the claimed protein contains the TM-CYT domain. See the specification at page 31 and Examples 4 and 5. Furthermore, the

specification discloses that the TM-CYT domain confers or restores fusogenic capability to the proteins. See page 8, lines 1-5. The specification also discloses that the CYT-TM domain causes syncytia formation through the recognition of a cell-surface receptor. See page 4, lines 5-20. Moreover, the specification disclóses in detail two protocols for performing the claimed method. See page 8, line 14 to page 9, line 2. Accordingly, in view of MPEP §2164.01(c), claim 39 satisfies the requirements of §112, second paragraph.

E. The term "derived" is not indefinite.

The Office Action asserts that the term "derived" renders claims that recite this term indefinite. Claims 38-40, 42 and 43 do not recite this term.

With regard to claim 41, the Office Action states that the term "derived" is vague and that the specification fails to provide a standard for ascertaining the requisite degree of derivation, which the Office Action asserts has may interpretations. Applicants respectfully disagree.

The American Heritage College Dictionary, 4th Edition, defines the term "derive" as: "to obtain or receive from a source." It would have been clear to one skilled in the art, based on the plain meaning of the term and on the specification at page 8, lines 7-12, that the feature "derived from tumor cell lines" means that the "derived" cells are cells obtained from a tumor cell line. Thus, claim 41 satisfies the requirements of §112, second paragraph.

V. ENABLEMENT REJECTIONS

The Office Action rejects claims 1-5 and 7-11 under the enablement requirement of §112, first paragraph. By this Amendment, claims 1-11 are canceled. In addition, new claims 38-43 satisfy the enablement requirements of §112, first paragraph, for at least the reasons discussed below.

Claim 38 recites:

> 38. A method for detecting the expression of an envelope protein of a human endogenous retrovirus, characterized in that the protein is selected from the group consisting of an envelope protein encoded by the human endogenous retrovirus HERV-W and a protein encoded by an open reading frame located on the chromosome 7 of the human genome, said method comprising:
>
> detecting a fusogenic power of said protein in cells of a cellular tissue or of a cell culture by observing formation of syncytia or an absence of formation of syncytia,
>
> wherein said detection is made in the presence of at least one cell-surface receptor.

Claims 39-43 depend from claim 1 and include all of its features.

The specification discloses that the claimed proteins cause, by cell-to-cell fusion, the formation of syncytia in various human and simian cell lines. The fusion phenomenon observed is dependent on the recognition of specific cell surface receptors. See the instant specification at page 4, lines 5-10 and 18-20. The specification further discloses that the region of the protein that is critical in allowing the protein to bind its receptor, leading to the formation of syncytia, is the TM + Cyt regions at amino acids 448-538 of SEQ ID NO: 1. See the instant specification at page 31, Example 4 and Figure 5. The specification also discloses two detailed protocols for the detection of the fusogenic power of the protein. See page 8, line 14 to page 9, line 2.

The test for enablement is whether one reasonably skilled in the art could make or use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation. MPEP §2164.01. MPEP §2164.01(a) provides a non-exhaustive, and non-dispositive, list of factors related to the enablement issue. In view of MPEP §2164.01 and 2164.01(a), in order for claims 38-43 to satisfy the enablement requirement of §112, first paragraph, the specification must enable one skilled in the art detect the expression of (i) an envelope protein encoded by the human endogenous retrovirus HERV-W or (ii) a protein encoded by an open reading frame located on the

chromosome 7 of the human genome. However, the specification need only enable the detection of a fusogenic power of said protein in cells of a cellular tissue or of a cell culture by observing formation of syncytia or an absence of formation of syncytia, in the presence of at least one cell-surface receptor.

A. (1) State of the Art and (2) Unpredictability

The Office Action states that it is unpredictable that any claimed fragment of SEQ ID NO: 1 would be able to induce syncytium formation. As an example, the Office Action cites a 7 amino acid Chlamydia protein sequence that is identical to amino acids 332-338 of SEQ ID NO: 1, yet has no fusogenic activity.

As discussed above, claims 38-43 all require detecting the expression of (i) an envelope protein encoded by the human endogenous retrovirus HERV-W or (ii) a protein encoded by an open reading frame located on the chromosome 7 of the human genome, by detecting a fusogenic power of said protein in cells of a cellular tissue or of a cell culture by observing formation of syncytia or an absence of formation of syncytia, in the presence of at least one cell-surface receptor. The specification discloses that the claimed proteins contain the TM-CYT domain. See the specification at page 31 and Examples 4 and 5. Furthermore, the specification discloses that the TM-CYT domain confers or restores fusogenic capability to the proteins. See page 8, lines 1-5. The specification also discloses that the CYT-TM domain causes syncytia formation through the recognition of a cell-surface receptor. See page 4, lines 5-20. Moreover, the specification discloses in detail two protocols for performing the claimed method. See page 8, line 14 to page 9, line 2.

Thus, in view of the considerable direction and guidance disclosed in the specification, it is predictable that the claimed proteins induce syncytia formation in the presence of receptor, such that one skilled in the art would have been enabled to practice the

claimed method without undue experimentation. Accordingly, claims 38-43 satisfy the enablement requirement of §112, first paragraph.

B. (3) Number of Working Samples and (4) Amount of Guidance

The Office Action states that the specification only enables cell-to-cell fusion observed between TELCeB6 cells transfected with the full-length HERV-W protein, and only in certain animal cell lines, since this is the only example disclosed in the specification.

However, MPEP 2164.02 states that compliance with the enablement requirement of §112, first paragraph, does not turn on whether an example is disclosed. MPEP 2164.08 further states that how a teaching is set forth, by specific example or broad terminology, is not important in determining whether the claims are enabled by the specification. In fact, MPEP § 2164.01(b) states that as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of §112, first paragraph, is satisfied.

As discussed above, the specification describes not only one, but two detection methods that bears a reasonable correlation to the entire scope of claim 38-43. See the specification at page 8, line 14 to page 9, line 2. Furthermore, although the MPEP states that working examples are not necessary to satisfy the enablement requirement of §112, first paragraph, the specification discloses four working examples of the claimed detection method. See Examples 1-4.

In addition, MPEP 2164.02 states that an example may be "working" or "prophetic," and defines a prophetic example as one that describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved. Thus, even though the disclosed working examples involve the use of human and simian cells, a prediction of results of the method used in other cells is not an enablement issue, under MPEP 2164.02.

Thus, the specification provides considerable direction and guidance such that one skilled in the art would have been enabled to practice the claimed method without undue experimentation. Accordingly, claims 38-43 satisfy the enablement requirement of §112, first paragraph.

C. (5) Scope of the Claims

The Office Action states that 1-5 and 7-11 encompass a method of detecting any fragment of SEQ ID NO: 1 in any cell line. However, new claims 38-43 clearly do not encompass a method of detecting any fragment of SEQ ID NO: 1 in any cell line.

As discussed above, claims 38-43 are directed to a method of detecting the expression of specific proteins by detecting syncytia formation (or absence thereof) in cells or cell culture, in the presence of a cell-surface receptor. Furthermore, as discussed above, the specification clearly enables the scope of claims 38-43. Specifically, the specification discloses that the claimed proteins contain the TM-CYT domain, which causes syncytia formation through the recognition of a cell-surface receptor. See the specification at page 4, lines 5-20, page 8, lines 1-5, page 31 and Examples 4 and 5. Moreover, the specification discloses in detail two protocols for performing the claimed method. See page 8, line 14 to page 9, line 2.

Thus, the specification bears a reasonable correlation to the scope of claims 38-43. Accordingly, claims 38-43 satisfy the enablement requirement of §112, first paragraph.

D. (6) Nature of the Invention and (7) Level of Skill in the Art

The Office Action states that the nature of the invention involves uninitiated experiments to mutate the 538 amino acid long peptide of SEQ ID NO: 1 in many ways and to detect the fusogenic activity afterward in any or all kinds of cell types. The Office Action identifies that a high level of skill is required in the art of plasmid mutagenesis, reconstruction and expression.

New claims 38-43 are clearly not directed to plasmid mutagenesis, reconstruction and expression. In contrast, claims 38-43 are directed to methods of detecting a fusogenic power of a protein in cells of a cellular tissue or of a cell culture by observing formation of syncytia or an absence of formation of syncytia, in the presence of at least one surface cell receptor. Furthermore, as discussed above, the specification discloses that the claimed proteins contain the TM-CYT domain, which causes syncytia formation through the recognition of a cell-surface receptor. See the specification at page 4, lines 5-20, page 8, lines 1-5, page 31. Moreover, the specification discloses in detail two protocols for performing the claimed method. See page 8, line 14 to page 9, line 2. The specification also discloses four working examples, Examples 1-4.

Thus, one skilled in the art would be able to practice the claimed detection method without undue experimentation, based on the considerable direction and guidance in the specification. Accordingly, claims 38-43 satisfy the enablement requirement of §112, first paragraph.

VI. REJECTION OVER JACOBS

The Office Action rejects claims 1-11 under §102(e) as being anticipated by U.S. Patent No. 6,312,921 B1 to Jacobs et al. (Jacobs). By this Amendment, claims 1-11 are canceled. In addition, claims 38-42 are not anticipated by Jacobs for at least the reasons discussed below.

Claim 38 recites: "detecting a fusogenic power of said protein in cells of a cellular tissue or of a cell culture by observing formation of syncytia or an absence of formation of syncytia, wherein said detection is made in the presence of at least one cell-surface receptor" (emphasis added). Jacobs fails to teach each and every feature of claim 38.

Jacobs discloses that AJ172_2 can mediate cell to cell fusion events leading to the formation of syncytia. See col. 55, lines 44-48. However, Jacobs also discloses that

> Fig. 7 demonstrates that the mechanism of AJ172_2 induced cell fusion does not require homophilic or heterophilic protein-protein interations.

(Emphasis added). See col. 56, lines 26-28. Jacobs fails to teach a step of detecting a fusogenic power of said protein in cells of a cellular tissue or of a cell culture by observing formation of syncytia or an absence of formation of syncytia, wherein said detection is made in the presence of at least one cell-surface receptor, as required by claim 38. Specifically, Jacobs teaches away from the claimed invention by disclosing that AJ172_2 mediates syncytia formation independent of at least one cell-surface receptor.

Accordingly, Jacobs fails to teach detecting syncytia, wherein the detection is in the presence of at least one cell surface receptor. For at least these reasons, Jacobs fails to teach every feature of claim 38, and claim 38 is not anticipated by Jacobs. Claims 39-42 depend from claim 38 and include all of its features. Accordingly, these dependent claims are not anticipated by Jacobs for at least the same reasons as claim 38.

Reconsideration and withdrawal of the rejection are respectfully requested.

VII. REJECTION OVER BLOND

The Office Action rejects claims 1-9 under §102(a) as being anticipated by Blond et al. (Blond). By this Amendment, claims 1-9 are canceled. In addition, claims 38-43 are not anticipated by Blond for at least the reasons discussed below.

Claim 38 is discussed above. Blond discloses detecting the expression of a specific HERV by Northern Blot. See page 1777, paragraphs 2-3. A Northern Blot detects expression by measuring the amount of mRNA present in a given cell. See, for example, Fig. 1. However, Blond fails to teach detecting a fusogenic power of said protein in cells of a cellular tissue or of a cell culture by observing formation of syncytia or an absence of formation of syncytia, wherein said detection is made in the presence of at least one cell-surface receptor, as required by claim 38. Accordingly, claim 38 is not anticipated by Blond.

Claims 39-43 depend from claim 38 and include all of its features. Accordingly, claims 39-43 are not anticipated by Blond for at least the same reasons as claim 38. Reconsideration and withdrawal of the rejection are respectfully requested.

VIII. 35 U.S.C. §102(b) REJECTION

The Office Action rejects claims 1-9 under §102(b) as being anticipated by Alliel et al. (Alliel). By this Amendment, claims 1-9 are canceled. In addition, claims 38-43 are not anticipated by Alliel for at least the reasons discussed below.

Claim 38 is discussed above. Alliel discloses the identification and characterization of HERV-7q transcripts. See the abstract, page 681 and Fig. 3. However, Alliel is silent regarding a detection method, and thus fails to teach detecting a fusogenic power of said protein in cells of a cellular tissue or of a cell culture by observing formation of syncytia or an absence of formation of syncytia, wherein said detection is made in the presence of at least one cell-surface receptor, as required by claim 38. Accordingly, claim 38 is not anticipated by Alliel.

Claims 39-43 depend from claim 38 and include all of its features. Accordingly, claims 39-43 are not anticipated by Alliel for at least the same reasons as claim 38. Reconsideration and withdrawal of the rejection are respectfully requested.

IX. CONCLUSION

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 38-43 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

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WPB:PAC

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